UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/963,288	11/03/97	NORSTEDT G	10806-48

HM12/0423

HOLLY D KOZLOWSKI
DINSMORE AND SHOHL
1900 CHEMED CENTER
255 EAST FIFTH STREET
CINCINNATI OH 45202

EXAMINER	
BAKER, A	
ART UNIT	PAPER NUMBER
1632	22

DATE MAILED: 04/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
08/963,288	Norstedt et al.
Examiner	**Art Unit**
Anne-Marie Baker, Ph.D.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Mar 26, 2001* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.

3. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search. (See NOTE below);

   (b) ☒ they raise the issue of new matter. (See NOTE below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: *See Item 1 on attached sheet.*

4. ☒ Applicant's reply has overcome the following rejection(s):
   NONE

5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).

6. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because:

7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):
   Claim(s) allowed: *NONE*
   Claim(s) objected to: *NONE*
   Claim(s) rejected: *1, 2, 5, 7-11, 15-17, 19-21, 23-32, 34-36, 39-42, and 44-54*

9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.

10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

11. ☐ Other:

JILL D. MARTIN
PRIMARY EXAMINER

Advisory Action

Item 1.

The new limitations raise the issue of new matter. Furthermore, the amendments to the claims would require new grounds of rejection under 35 U.S.C. 112, second paragraph.

With regard to Claims 1, 2, 19-21, 34-36, 39-42, and 46-52, the new limitations raise the issue of new matter. The claims are directed to a method of enhancing transcription *in vitro*. The claims now recite that the host cell will be transfected to incorporate the enhancer element upstream of the promoter. Thus, site-specific integration of the element is required. However, the specification does not contemplate performing site-specific integration. As recited in the preamble, a DNA construct comprising a structural gene and a promoter upstream of the structural gene is already incorporated in the genome of the host cell. **Then** the cell is transfected "to incorporate" six copies (or at least one) of an enhancer element upstream of the promoter. Gene targeting (*i.e.*, homologous recombination) is required to accomplish this site-specific incorporation of DNA into the genome of the host cell. However, the specification as-filed does not contemplate using gene targeting or homologous recombination to produce this result, wherein the enhancer element is incorporated into a specific site within the genome, *i.e.* upstream of the promoter. The specification must provide proper support for the method as claimed. No support is provided in the specification for incorporating the enhancer element into the genome of a host cell using gene targeting. The specification does not contemplate incorporating the enhancer element at a specific site within the genome, nor does it contemplate how this would be accomplished. Further, with regard to the enablement rejection as previously advanced, the claimed method would not work as the method steps do not recite the use of gene targeting techniques, such as the use of appropriate flanking sequences to permit homologous recombination

at the requisite site (see page 3 of the Office Action of Paper No. 19). Moreover, the specification itself does not contemplate doing this. Thus, as explained at page 3 of Paper No. 19, the enhancer element, consisting of the nucleotide sequence TTCTGAGAA, as recited in amended Claim 19, would be randomly incorporated into the genome of the host cell. Given that proper support in the specification is absent, this rejection cannot be overcome by reciting the necessary steps and elements for site-specific integration, as this would constitute new matter. The specification only discloses transfection of recombinant constructs that already include the enhancer element.

With regard to Claims 8-10, a new rejection under 35 U.S.C. 112, second paragraph would be required because the claim recites "six copies" of an enhancer element, but then the claim goes on to recite "wherein at least one of the copies of the enhancer element consists essentially of the nucleotide sequence TTCTGAGAA." Thus, only one copy is required to consist essentially of the nucleotide sequence TTCTGAGAA. The other copies can be any enhancer element. However, the term copy clearly indicates that all six elements are identical, i.e. copies. Thus, the claim language is completely contradictory. It is unclear how the six elements can be considered copies if they are not all the same thing. Claim 10 goes on to recite the limitation "wherein at least one other copy of the enhancer element is the nucleotide sequence SEQ ID NO: 1." It is unclear how one copy of the enhancer element can consist essentially of the nucleotide sequence TTCTGAGAA while another copy is the nucleotide sequence of SEQ ID NO: 1, and yet both elements are still be considered copies. At pages 7-8 of Applicants response (Paper No. 21), Applicants assert that "[a]s these claims recite **different copies** of the enhancer element, it is believed that claims 8 and 10, and claim 17 which depends from claim 10, are definite..." (emphasis added). This terminology is clearly indefinite because **copies** are **identical**, not **different**. It is unclear how **copies** can be **different**.

As amended, Claims 27-32 recite the new limitation "wherein the enhancer element is incorporated with the structural gene by construction." A new rejection under 35 U.S.C. 112, second paragraph would be required because it is unclear how the enhancer element is "incorporated with the structural gene by construction."